Pooling Data on Pools

Genotoxicity of Chemicals in Indoor Swimming Pools

Disinfection by-products (DBPs) form in swimming pool water from reactions between disinfectants such as chlorine and organic matter such as sweat, skin cells, and urine. A new study described in a set of three articles provides the first comprehensive characterization of DBPs in an indoor pool environment and offers initial evidence of cellular-level effects of these chemicals in swimmers in an indoor chlorinated pool [***EHP* 118(11):1523–1530; Richardson et al.**; ***EHP* 118(11):1531–1537, Kogevinas et al.**; ***EHP* 118(11):1538–1544, Font-Ribera et al.**].

Markers of genotoxicity and mutagenicity were detected in swimmers after 40 minutes in the pool.

The authors assessed short-term changes in 49 healthy adults after they swam for 40 minutes in a public indoor chlorinated pool. They observed increases in two biomarkers of genotoxicity relative to the concentration of brominated trihalomethanes (THMs) in exhaled breath, which were used as a proxy of the swimmers' total DBP exposures. Those biomarkers were micronuclei in blood lymphocytes (which have been associated with cancer risk in healthy subjects) and urine mutagenicity (a biomarker of exposure to genotoxic agents).

The team also took detailed measurements of THMs in air around the pool and in exhaled breath of the swimmers before and after swimming. The investigators measured several biomarkers of respiratory effects after swimming and found changes in only one—a slight increase in serum CC16, which suggests an increase in lung epithelium permeability. However, they found no evidence that DBP exposure affected lung function.

The research team identified more than 100 DBPs in the water of the chlorinated pool as well as another indoor pool disinfected with bromine. Some of these compounds had never been reported previously in swimming pool water and/or chlorinated drinking water. *In vitro* assays showed the swimming pool water was mutagenic at levels similar to that of drinking water but was more cytotoxic (could kill cells at a lower concentration) than drinking water.

The researchers acknowledge the need for further research on a variety of swimming pools under various conditions of maintenance and use as well as more complete evaluations of the uptake and potential effects of the compounds present in pool water. They also note the importance of timing in the collection of biological samples—a parameter for which there was no precedent, given the lack of previous studies of this type with swimmers. Above all, they emphasize that positive health effects of swimming can be maintained by minimizing pool levels of DBPs.

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Opening the Window to Cancer

Potential Mechanism behind Increased Susceptibility in Rats Exposed Prenatally to BPA

Exposure to environmental factors before birth or during other critical periods of development can cause subtle changes in a tissue's molecular foundations, leading to health effects later in life. Prenatal exposure to bisphenol A (BPA) is linked to cellular and structural changes in the mammary glands of adult rats and increased susceptibility to chemically induced cancer. New research now suggests a possible mechanism of action for this increase in cancer susceptibility via altered protein expression patterns in rat mammary gland tissue [***EHP* 118(11):1614–1619; Betancourt et al.**].

Pregnant rats were exposed to 0, 25, or 250 μg BPA/kg/d from day 10 to 21 postconception, and their female offspring were given a single dose of the cancer-inducing compound dimethylbenzanthracene (DMBA) at 50 or 100 days after birth (i.e., young adulthood). Experiments were conducted to determine the relationship between prenatal BPA exposure and the expression of proteins intrinsic to the growth and development of the mammary gland in adulthood. These proteins included estrogen receptor-α (ER-α); PR and Bcl-2, downstream targets of ER-α; steroid receptor coactivators (SRCs) 1 to 3, which influence ER-α transcriptional activity; and several growth factor receptors and signaling molecules that direct cell proliferation and programmed death.

Body weight and hormonally sensitive end points (time to vaginal opening, serum levels of the hormones 17β estradiol and progesterone, and estrous cyclicity) were assessed but found to be unchanged in relation to prenatal BPA exposure. ER-α, PR, and Bcl-2 were significantly downregulated and SRC-3 and some signaling molecules were upregulated in rats exposed prenatally to BPA.

DMBA administered to rats at 50 days did not yield significant differences in tumor incidence between those with or without prenatal BPA exposure. Among animals that received DMBA at 100 days, all assayed proteins were significantly upregulated in the BPA-exposed rats, and cell proliferation was enhanced, but apoptosis was unchanged. These animals also had decreased time to tumor formation and increased tumor incidence and severity.

These findings suggest that prenatal exposure to BPA in rats alters expression of key receptors and components of cellular signaling pathways in the mammary gland in adulthood, consequently increasing the tissue's susceptibility to chemically induced cancer. Whether this occurs in humans is unknown. Data from the Centers for Disease Control and Prevention indicate human exposure to the chemical is widespread, with approximately 95% of Americans estimated to have detectable levels of BPA metabolites in their urine. Continued research is necessary to elucidate the mechanisms by which BPA exposure early in life influences the development of permanent effects in maturity.

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Disinfection By-products and Bladder Cancer

Common Genetic Variants May Confer Increased Risk

Disinfection of the water supply is an important and cost-effective tool to reduce morbidity and mortality from a wide range of infectious diseases. However, the chemicals used to treat water also can produce potentially toxic compounds known as disinfection by-products (DBPs). A new study shows strong associations between DBP exposure and bladder cancer among individuals who carry inherited variants in three genes (*GSTT1*, *GSTZ1*, and *CYP2E1*) that code for key enzymes that metabolize DBPs [***EHP* 118(11):1545–1550; Cantor et al.**].

DBPs form when disinfectants (such as chlorine) react with organic matter that collects in water (such as algae or humic acids from decayed leaves). Most DBP exposure is due to ingestion of drinking water, although some DBPs can be inhaled or absorbed through the skin during bathing, showering, or swimming in a pool. Laboratory studies show that many DBPs are mutagenic or carcinogenic, but epidemiologic studies to date have revealed only a modest association between DBP exposure and cancer in humans.

In the present study, 595 men and 85 women newly diagnosed with bladder cancer were recruited from 18 hospitals in Spain and matched with controls (622 men and 92 women) who had been hospitalized with conditions thought to be unrelated to bladder cancer. The authors estimated DBP exposure since age 15 years by linking participants' residential histories with documented and estimated levels of trihalomethanes (THMs)—a DBP often used as a marker for total DBP exposure—in municipal water systems. Participants were genotyped for variations in *GSTT1*, *GSTZ1*, and *CYP2E1*.

Across the study population cancer risk nearly doubled between the highest and lowest levels of DBP exposure, and the association with DBP exposure was even stronger among participants who carried one of three variant genotypes. Smokers also had a higher risk (smoking is the most significant known risk factor for bladder cancer).

One of the genotypes appeared to increase the association between DBPs and bladder cancer codes for the active form of the enzyme glutathione transferase theta-1 (GSTT1), which metabolizes brominated THMs to mutagens. Another increases the activity of cytochrome P450 2E1 (CYP2E1), which catalyzes the primary oxidation of THMs. There is evidence the third genotype may reduce the activity of glutathione transferase zeta-1 (GSTZ1), which transforms haloacetic acids, another type of DBP, to less toxic compounds.

Among individuals who carried both of the *GSTT1* and *GSTZ1* genotypes noted above (28% of study participants), those with the highest DBP exposure were at a 1.5 times increased risk of bladder cancer compared with carriers with the lowest DBP exposure. These genotypes are relatively common, occurring jointly in more than 20% of the controls in the study population. The findings from this study therefore may have significant public health implications for cancer prevention.

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A Balanced Diet?

Selenium May Offset the Effects of Methylmercury on Cataract Development

Dietary exposure to mercury from fish has been posited as a risk factor for cataracts because some reports have suggested methylmercury accumulates in the lens of the eye. But selenium from other dietary sources may offset that damage, according to a study of communities in the Amazon basin [***EHP* 118(11):1584–1589; Lemire et al.**]. The findings, while preliminary, hint at potential public health measures in areas where methylmercury-contaminated fish are a significant part of people's diets.

With old age comes cataracts, particularly in latitudes like the Amazon, where higher ultraviolet radiation exposure and other environmental factors contribute to the clouding of the lenses in human eyes. And while surgical fixes exist for cataracts, people in isolated regions may not always have access to those options. Cataracts therefore are a major cause of blindness among older people in the Amazon.

The current study involved communities that eat fish from the Tapajós River, a tributary of the Amazon. People here have among the highest reported exposures to mercury in the world. Deforestation in the region leads to the release of natural inorganic mercury from soils into surface waters, where it is methylated and eventually ends up in fish.

Several hundred people voluntarily participated in the study, which entailed taking an overnight boat trip to a nearby city where participants gave blood samples and were examined by optometrists. In the end, 211 people over age 40 were included in the analysis. A third of them had age-related cataracts.

Low plasma selenium and high blood mercury each were associated with a higher prevalence of cataracts (over 2 and 4 times higher, respectively). The team calculated that the people with both low plasma selenium and high blood mercury were 16 times more likely to develop cataracts than the "optimum situation" group, which had both high plasma selenium and low blood mercury.

This is the first study known to associate high levels of methylmercury from fish consumption with increased occurrence of cataracts. The authors emphasize that other factors—such as differences in dietary intakes of antioxidants and vitamins—could confound their findings. Still, if the observed associations hold true in broader studies, public health interventions to alleviate cataracts in this Amazonian population must consider both the health benefits of fish consumption and the risks of the main source of dietary selenium in the region: brazil nuts, which also contain barium and strontium, heavy metals with their own hazards.

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Women and children from a Tapajós village clean fish, a chief component of the local diet, which also includes rice, manioc flour, fruits, and brazil nuts.

Mélanie Lemire